

Docket No.: 58532-012

PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Arthur L. HERBST, et al.

Serial No.: 09/884,466

: Group Art Unit: 1614

Filed: June 20, 2001

: Examiner: Vickie Kim

For: COX-2 INHIBITORS AND THE PREVENTION OF THE SIDE EFFECTS OF  
RADIATION THERAPYDECLARATION UNDER 37 CFR 1.132Commissioner for Patents  
Washington, DC 20231

Sir:

I, Dr. Ralph R. Weichselbaum, declare and say as follows:

1. That I am one of the inventors named in the above-identified application Serial No. 09/884,466 and I am also an inventor named in U.S. Patent 5,641,755, entitled "Regulation of X-Ray Mediated Gene Expression";

2. I am familiar with the prosecution of this application Serial No. 09,884,466 and I have read and understand the Official Action dated April 24, 2002 in this application.

3. As I understand the patent Examiner's position, the Examiner considers that the claims of the application are either anticipated or obvious over U.S. Patent 5,972,986 to Siebert et al. considered alone or in combination with certain additional patents including my prior U.S. Patent 5,641,755.

4. In the Siebert U.S. Patent 5,972,986, I note that Siebert mentions in column 2, lines 59-61, that the COX-2 inhibitors disclosed in this patent "can also be used to treat the fibrosis which occurs with radiation therapy". It is believed well understood in the medical art that fibrosis is a later effect of radiation therapy that has no relation to the side effects from radiation treatment now claimed in this patent application. None of the side effects recited in the broadest claim 1 of this patent application has any relationship to fibrosis and in my opinion, one would not be obvious in view of the other. Therefore, in my opinion, Siebert does not contain any suggestion for the use of COX-2 inhibitors to reduce one or more of the side effects claimed in this patent application.

5. The patent Examiner has also indicated that it would have been obvious to one of ordinary skill in the art to use COX-2 inhibitors to reduce the specific side effects now recited in the claims of this patent application. Included in this rejection by the Examiner is reliance on my prior U.S. Patent 5,641,755 as disclosing a teaching regarding radiation induced side effects and inflammatory cytokines. The patent Examiner relies on this patent as teaching that cytokines are responsible for the acute and sub-acute radiation induced side effects and inflammatory cytokine production is mediated by the prostaglandin/arachidonic metabolic pathway. The Examiner states that "Weichselbaum states that radiation-induced side effects could be effectively reduced by the inhibition of said metabolic pathway which attenuates the production of cytokines such as TNF-". Further, the Examiner states that Weichselbaum further teaches various radiation exposures to different locations to treat specific tumors referring to column 7.

6. While these broad statements can be found in my prior patent, these statements have nothing to do with the claims made in this patent application for reducing one or more specific side-effects resulting from radiation treatment. There is nothing in my prior patent which would suggest that COX-2 inhibitors would have the utility described in the claims of this patent application. My prior patent was concerned with methods of inhibiting the production of cytokines following exposure of cells to ionizing radiation. In the disclosure of my prior patent, cells are treated with lipoxygenase prior to exposure to ionizing radiation and the preferred lipoxygenase is ketoconazole. This has nothing to do with the invention claimed in this patent application. There is no disclosure in my prior patent for use of any COX-2 inhibitor to reduce any side effects resulting from radiation treatment. Further, the disclosed invention in my prior patent would not lead one of skill in the art in my opinion to the invention claimed in this application of using COX-2 inhibitors to reduce side effects resulting from radiation treatment.

7. It is therefore my opinion that there is nothing in the prior Weichselbaum patent or the other references relied on by the Examiner which would motivate one of skill in the art to believe that Siebert's teaching that COX-2 inhibitors may be used to treat fibrosis resulting from radiation treatment to the claimed invention of reducing the specific side effects resulting from radiation treatment as set forth in our claims in this patent application. It is therefore my opinion as one of skill in this art that the method of reducing the specific side effects as claimed in this application would not be obvious in view of Siebert or in any combination of Siebert with my prior patent or the other references relied on by the Examiner.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

DateAug 22, 2002  
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Dr. Ralph Weichselbaum